

1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide; 5-(S)-benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide; 5-(R)-benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide; 1-benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide; and 1-benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide; among others.

**In The Claims:**

A marked-up version of the claims showing the amendments is attached hereto as Exhibit B. Matter that has been deleted from the claims is indicated by brackets and matter that has been added is indicated by underlining.

Please cancel Claims 21, 22, and 26-28 without prejudice to or disclaimer of the subject matter contained therein.

Please enter the following amended claims:

1. (Twice Amended) A method of inhibiting apoptosis in a subject, comprising:  
*B2* administering a therapeutically effective amount of at least one serine protease inhibitor in which the effective amount inhibits apoptosis;

wherein the subject suffers from at least one of wasting disease, Alzheimer's disease, arthritis, muscular dystrophy, Downs Syndrome, sepsis, HIV infection, multiple sclerosis, arteriosclerosis, diabetes, autoimmune disease, ischemia-reperfusion injury, or toxin-induced liver injury.

3. (Amended) The method of Claim 1, in which the serine protease inhibitor is  $\alpha_1$ -antitrypsin, an oxidation-resistant or free radical-resistant variant thereof, or combinations thereof.

4. (Twice Amended) The method of Claim 3 in which the effective amount is at least .001 and no greater than 70 g/kg body weight.

8. (Twice Amended) The method of Claim 1, in which the serine protease inhibitor is selected from the group consisting of:

- i. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- ii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2-phenylethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- iii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2-methoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- iv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trifluoromethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

v. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(methyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

vi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(difluoromethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

vii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(benzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

viii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-methoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

ix. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2,6-difluorobenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

x. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trans-styryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trans-4-trifluoromethylstyryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trans-4-methoxystyryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xiii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-thienylmethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xiv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(phenyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenylpropyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide.

xvi. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide (also known as CE-2072);

xvii. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(3-(methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xviii. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(methyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xix. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(3-trifluoromethylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xx. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(4-dimethylaminobenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;  
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xxi. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(1-naphthyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxii. (benzyloxycarbonyl)-L-valyl-[1-(3-(5-(3,4-methylenedioxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxiii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-dimethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxiv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-dimethoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-ditrifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxvi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-methylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxvii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(biphenylmethine)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxviii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(4-phenylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxix. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxx. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(cyclohexylmethylen)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

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xxxii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethyldimethylmethylen)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxiii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(1-naphthylmethylen)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxiv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-pyridylmethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-diphenylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxvi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(4-dimethylaminobenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxvii. 2-(5-[(benzyloxycarbonyl)amino]-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-(S)-2-methylpropyl]acetamide;

xxxviii. 2-(5-amino-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

xxxix. 2-[5-[(benzyloxycarbonyl)amino]-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-(S)-2-methylpropyl]acetamide;

xl. 2-[5-amino-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-methylpropyl]acetamide;

xli. (pyrrole-2-carbonyl)-N-(benzyl)glycyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

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xlii. (pyrrole-2-carbonyl)-N-(benzyl)glycyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)(1,2,4-oxadiazolyl)-(S)-methylpropyl]amide;

xliii. (2S,5S)-5-amino-1,2,4,5,6,7-hexahydroazepino-[3,2,1]-indole-4-one-carbonyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-(R,S)-2-methylpropyl]amide;

xliv. BTD-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlv. (R,S)-3-amino-2-oxo-5-phenyl-1,4-benzodiazepine-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

xlvi. (benzyloxycarbonyl)-L-valyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlvii. (benzyloxycarbonyl)-L-valyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlviii. acetyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlix. 3-(S)-(benzyloxycarbonyl)amino- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

l. 3-(S)-(amino)- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide trifluoroacetic acid salt;

li. 3-(S)-[(4-morpholinocarbonyl-butanoyl)amino]- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(R,S)-methylpropyl]acetamide;

lii. 6-[4-fluorophenyl]- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

liii. 2-(2-(R,S)-phenyl-4-oxothiazolidin-3-yl]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lvi. 2-(2-(R,S)-benzyl-4-oxothiazolidin-3-yl]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lvii. 2-(2-(R,S)-benzyl-4-oxothiazolidin-3-yl oxide]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(R,S)-methylpropyl]acetamide;

lviii. (1-benzoyl-3,8-quinazolinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lix. (1-benzoyl-3,6-piperazinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lx. (1-phenyl-3,6-piperazinedione)-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)]-2-(S)-methylpropyl]acetamide;

lxi. 3-[(benzyloxycarbonyl)amino]-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxii. 3-[(benzyloxycarbonyl)amino]-7-piperidinyl-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxiii. 3-(carbomethoxy-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxiv. 3-(amino-quinolin-2-one)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

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lxv. 3-[(4-morpholino)aceto]amino-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxvi. 3,4-dihydro-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxvii. 1-acetyl-3-(4-fluorobenzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxviii. 1-acetyl-3-(4-dimethylaminobenzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxix. 1-acetyl-3-(4-carbomethoxybenzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxx. 1-acetyl-3-[(4-pyridyl)methylene]piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxi. 4-[1-benzyl-3-(R)-benzyl-piperazine-2,5-dione]-N-[1-(2-[5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxii. 4-[1-benzyl-3-(S)-benzylpiperazine-2,5-dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxiii. 4-[1-benzyl-3(R)-benzylpiperazine-2,5-dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxiv. 4-[1-benzyl-3-(S)-benzylpiperazine-2,5-dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxv. 4-[1-benzyl-3-(S)-benzylpiperazine-2,5-dione]-N-[1-(3-(5-(2-dimethylaminoethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide; *B5*

lxxvi. 4-[1-methyl-3-(R,S)-phenylpiperazine-2,5-dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxvii. 4-[methyl-3-(R,S)-phenylpiperazine-2,5-dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxviii. 4-[1-(4-morpholinoethyl)-3-(R)-benzylpiperazine-2,5-dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxix. 5-(R,S)-phenyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxx. 5-(R)-benzyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxi. 5-(S)-benzyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxii. 5-(S)-benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxiii. 5-(R)-benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxiv. 1-benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

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lxxxv. 1-benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

pharmaceutically acceptable salts thereof;

and combinations thereof.

9. (Twice Amended) The method of Claim 8, in which the effective amount is at least 0.001 and no greater than 7.0 g/kg body weight.

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12. (Twice Amended) The method of Claim 1, in which the therapeutically effective amount is sufficient to provide at least 10 pM and no greater than 2 mM of the inhibitor in the biological fluid of the subject.

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14. (Twice Amended) The method of Claim 1, in which the therapeutically effective amount is sufficient to provide at least .5  $\mu$ M and no greater than 200  $\mu$ M in the biological fluid of the subject.

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16. (Twice Amended) The method of Claim 1, in which the therapeutically effective amount is administered at least once daily and no more than once hourly.

18. (Amended) A method of prophylactically treating an individual at risk for a pathological condition that is precipitated at least in part by excessive apoptosis, comprising:

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administering to an individual a therapeutically effective amount of at least one serine protease inhibitor.

19. (Amended) A method for reducing apoptosis in an *in vitro* mammalian cell culture, an *ex vivo* mammalian tissue culture, or mammalian organ comprising:

providing to a cell culture, tissue culture, or organ an amount of a serine protease inhibitor sufficient to inhibit apoptosis in said cell culture, tissue culture, or organ wherein a measured amount of apoptosis is indicative of apoptosis activity.

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23. (Twice Amended) The method of Claim 25, in which the serine protease inhibitor is derivatized by esterification, acetylation, or amidation, and wherein the derivatized serine protease inhibitor retains the inhibitory activity.

24. (Twice Amended) The method of Claim 25, wherein the at least one cell is a cell of a subject, and wherein the amount is sufficient to bring the concentration of serine protease inhibitor in the subject's blood to at least .5  $\mu$ M and no greater than 200  $\mu$ M.

25. (Twice Amended) A method of inhibiting apoptosis, comprising providing a serine protease inhibitor to at least one cell and measuring a decrease in apoptosis, wherein the serine protease inhibitor is an oxidation-resistant or free radical-resistant variant of  $\alpha_1$ -antitrypsin; or:

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- i. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- ii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2-phenylethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- iii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2-methoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- iv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trifluoromethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- v. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(methyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- vi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(difluoromethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;
- vii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(benzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

viii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-methoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

ix. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(2,6-difluorobenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

x. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trans-styryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trans-4-trifluoromethylstyryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(trans-4-methoxystyryl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

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xiii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-thienylmethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xiv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(phenyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenylpropyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide.

xvi. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide (also known as CE-2072);

xvii. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(3-(methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xviii. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(methyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xix. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(3-trifluoromethylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xx. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(4-dimethylaminobenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxi. (benzyloxycarbonyl)-L-valyl-N-[1-(2-(5-(1-naphthyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxii. (benzyloxycarbonyl)-L-valyl-[1-(3-(5-(3,4-methylenedioxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxiii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-dimethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxiv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-dimethoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-ditrifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxvi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-methylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxvii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(biphenylmethine)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxviii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(4-phenylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxix. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxx. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-phenoxybenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(cyclohexylmethylen)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethyldimethylmethylen)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxiii. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(1-naphthylmethylen)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxiv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-pyridylmethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxv. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3,5-diphenylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxvi. (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(4-dimethylaminobenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]-L-prolinamide;

xxxvii. 2-(5-[(benzyloxycarbonyl)amino]-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-(S)-2-methylpropyl]acetamide;

xxxviii. 2-(5-amino-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

xxxix. 2-[5-[(benzyloxycarbonyl)amino]-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-(S)-2-methylpropyl]acetamide;

xl. 2-[5-amino-6-oxo-2-(4-fluorophenyl)-1,6-dihydro-1-pyrimidinyl]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-methylpropyl]acetamide;

xli. (pyrrole-2-carbonyl)-N-(benzyl)glycyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlii. (pyrrole-2-carbonyl)-N-(benzyl)glycyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)(1,2,4-oxadiazolyl)-(S)-methylpropyl]amide;

xliii. (2S,5S)-5-amino-1,2,4,5,6,7-hexahydroazepino-[3,2,1]-indole-4-one-carbonyl-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-(R,S)-2-methylpropyl]amide;

xliv. BTD-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

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xlv. (R,S)-3-amino-2-oxo-5-phenyl-1,4-benzodiazepine-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

xlvi. (benzyloxycarbonyl)-L-valyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlvii. (benzyloxycarbonyl)-L-valyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(3-(5-(3-trifluoromethylbenzyl)(1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlviii. acetyl-2-L-(2,3-dihydro-1H-indole)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]amide;

xlix. 3-(S)-(benzyloxycarbonyl)amino- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

l. 3-(S)-(amino)- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide trifluoroacetic acid salt;

li. 3-(S)-[(4-morpholinocarbonyl-butanoyl)amino]- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(R,S)-methylpropyl]acetamide;

lii. 6-[4-fluorophenyl]- $\epsilon$ -lactam-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

liii. 2-(2-(R,S)-phenyl-4-oxothiazolidin-3-yl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

liv. 2-(2-(R,S)-phenyl-4-oxothiazolidin-3-yl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl(hydroxymethyl)-2-(S)-methylpropyl]acetamide;

lv. 2-(2-(R,S)-benzyl-4-oxothiazolidin-3-yl)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lvi. 2-(2-(R,S)-benzyl-4-oxothiazolidin-3-yloxide]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(R,S)-methylpropyl]acetamide;

lvii. (1-benzoyl-3,8-quinazolinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lviii. (1-benzoyl-3,6-piperazinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lix. (1-phenyl-3,6-piperazinedione)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lx. (1-phenyl-3,6-piperazinedione)-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)]-2-(S)-methylpropyl]acetamide;

lxi. 3-[(benzyloxycarbonyl)amino]-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxii. 3-[(benzyloxycarbonyl)amino]-7-piperidinyl-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxiii. 3-(carbomethoxy-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxiv. 3-(amino-quinolin-2-one)-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxv. 3-[(4-morpholino)aceto]amino-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxvi. 3,4-dihydro-quinolin-2-one-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxvii. 1-acetyl-3-(4-fluorobenzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxviii. 1-acetyl-3-(4-dimethylaminobenzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxix. 1-acetyl-3-(4-carbomethoxybenzylidene)piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxx. 1-acetyl-3-[(4-pyridyl)methylene]piperazine-2,5-dione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxi. 4-[1-benzyl-3-(R)-benzyl-piperazine-2,5-dione]-N-[1-(2-[(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxii. 4-[1-benzyl-3-(S)-benzylpiperazine-2,5-dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxiii. 4-[1-benzyl-3(R)-benzylpiperazine-2,5-dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxiv. 4-[1-benzyl-3-(S)-benzylpiperazine-2,5-dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxv. 4-[1-benzyl-3-(S)-benzylpiperazine-2,5-dione]-N-[1-(3-(5-(2-dimethylaminoethyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxvi. 4-[1-methyl-3-(R,S)-phenylpiperazine-2,5-dione]-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxvii. 4-[methyl-3-(R,S)-phenylpiperazine-2,5-dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxviii. 4-[1-(4-morpholinoethyl)-3-(R)-benzylpiperazine-2,5-dione]-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxix. 5-(R,S)-phenyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxx. 5-(R)-benzyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxi. 5-(S)-benzyl-2,4-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxii. 5-(S)-benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxiii. 5-(R)-benzyl-2,4-imidazolidinedione-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxiv. 1-benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(2-(5-(3-methylbenzyl)-1,3,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

lxxxv. 1-benzyl-4-(R)-benzyl-2,5-imidazolidinedione-N-[1-(3-(5-(3-

*B10* trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl)-2-(S)-methylpropyl]acetamide;

pharmaceutically acceptable salts thereof;

or combinations thereof.

Please add the following new claims:

29. (New) The method of Claim 1 wherein said wasting disease includes neurodegenerative disease, myocardial infarction, and stroke.

*B11*  
30 (New) The method of Claim 1 wherein the serine protease inhibitor inhibits at least one of trypsin, cathepsin G, tryptase TL-2, factor Xa, elastase, or proteinase-3.

REMARKS

Claims 1-10 and 12-28 were pending in the application. Claims 26-28 are hereby cancelled without prejudice to pursuing the cancelled claims in this or other continuing applications. Claims 1, 3, 4, 8, 9, 12, 14, 16, 18, 19, 24, and 25 have been amended. New Claims 29 and 30 have been added. Upon entry of these amendments, Claims 1-10, 12-20, 23-25, and 29-30 will be pending and under active consideration. Claims 1, 18, 19, and 25 are independent.